

In the Claims:

1. (Original) A coupling agent comprising 6-chloro-1-hydroxybenzotriazol-1-yl-N-oxy-tris(pyrrolidino)phosphonium hexafluorophosphate.

2. (Original) A process of preparing 6-chloro-1-hydroxybenzotriazol-1-yl-N-oxy-tris(pyrrolidino)phosphonium hexafluorophosphate, the process comprising:
 providing tris-(1-pyrrolidino)phosphonium hexafluorophosphate;
 providing 6-chloro-1-hydroxybenzotriazole; and
 reacting tris-(1-pyrrolidino)phosphonium hexafluorophosphate and 6-chloro-1-hydroxybenzotriazole, thereby obtaining 6-chloro-1-hydroxybenzotriazol-1-yl-N-oxy-tris(pyrrolidino)phosphonium hexafluorophosphate.

3. (Original) The process of claim 2, wherein said reacting is performed in the presence of a base.

4. (Original) The process of claim 2, wherein said reacting is performed in the presence of an organic solvent.

5. (Original) The process of claim 2, wherein providing said tris-(1-pyrrolidino)phosphonium hexafluorophosphate comprises:
 providing tris-(1-pyrrolidine)phosphine oxide;
 converting said tris-(1-pyrrolidine)phosphine oxide to tri-pyrrolidin-1-yl-phosphonium chloride; and
 reacting said tri-pyrrolidin-1-yl-phosphonium chloride with potassium hexafluorophosphate.

6. (Original) The process of claim 2, wherein the 6-chloro-1-hydroxybenzotriazol-1-yl-N-oxy-tris(pyrrolidino)phosphonium hexafluorophosphate is obtained in a purity that is equal to or is greater than 96 %.

7. (Original) A method of synthesizing a peptide, the method comprising:
 sequentially coupling a plurality of amino acids, one with another, in the presence of 6-chloro-1-hydroxybenzotriazol-1-yl-N-oxy-

tris(pyrrolidino)phosphonium hexafluorophosphate, to thereby obtain a peptide containing said plurality of amino acids.

8. (Original) The method of claim 7, wherein at least one of said amino acids is selected from the group consisting of an amino acid having a secondary alpha amine, an amino acid having a tertiary alpha amine, an amino acid having a substituted alpha carbon atom and an amino acid having an amino-containing side chain.

9. (Original) The method of claim 7, wherein at least one of said amino acids is selected from the group consisting of an amino acid having a secondary alpha amine and an amino acid having a tertiary alpha amine.

10. (Original) The method of claim 7, wherein at least one of said amino acids is an amino acid having a substituted alpha carbon atom.

11. (Original) The method of claim 7, wherein at least two coupled amino acids in said peptide are amino acids having a substituted alpha carbon atom.

12. (Currently Amended) The method of ~~claims 10 and 11~~ claim 10, wherein said alpha carbon is substituted by an alkyl.

13. (Original) The method of claim 7, wherein at least one of said amino acids is an amino acid having an amino-containing side chain.

14. (Original) The method of claim 7, wherein at least two coupled amino acids in said peptide are amino acids having an amino-containing side chain.

15. (Currently Amended) The method of ~~claims 13 or 14~~ claim 13, wherein said amino acid having an amino-containing side chain is arginine.

16. (Original) The method of claim 9, wherein said peptide is obtained in a yield greater than 10 %.

17. (Currently Amended) The method of ~~claims 10 and 11~~ claim 10, wherein said peptide is obtained in a yield greater than 90 %.

18. (Currently Amended) The method of ~~claims 13 and 14~~ claim 13, wherein said peptide is obtained in a yield greater than 80 %.

19. (Original) The method of claim 7, wherein synthesizing said peptide is effected by a solid phase synthesis.

20. (Original) A crude composition of peptides, said peptides being synthesized in a C-terminus to N-terminus direction, the composition consisting essentially of a peptide having a desired amino acid sequence and a plurality of peptides having undesired amino acid sequences and being impurities to said peptide having said desired amino acid sequence, wherein a concentration of said peptide having said desired amino acid sequence in said composition is at least 5 % above a concentration of an identical peptide having said desired amino acid sequence in a composition of peptides being synthesized in said C-terminus to N-terminus direction using benzotriazol-1-yl-N-oxy-tris(pyrrolidino)phosphonium hexafluorophosphate as a coupling agent otherwise prepared under identical conditions.

21. (Original) The crude composition of peptides of claim 20, wherein said peptide having said desired amino acid sequence comprises at least one amino acid residue selected from the group consisting of a residue of an amino acid having a secondary alpha amine, a residue of an amino acid having a tertiary alpha amine, a residue of an amino acid having a substituted alpha carbon atom and a residue of an amino acid having an amino-containing side chain.

22. (Original) The crude composition of peptides of claim 21, wherein said peptide having said desired amino acid sequence comprises at least two coupled amino acid residues, whereby at least one of said at least two amino acid residues is selected from the group consisting of a residue of an amino acid having a secondary alpha amine and a residue of an amino acid having a tertiary alpha amine.

23. (Currently Amended) The crude composition of peptides of ~~claims 21 and 22~~ claim 21, wherein said amino acid having a secondary alpha amine is N-methylvaline.

24. (Original) The crude composition of peptides of claim 21, wherein said peptide having said desired amino acid sequence comprises at least two coupled amino acid residues acids having a substituted alpha carbon atom.

25. (Currently Amended) The crude composition of peptides of ~~claims 21 and 24~~ claim 21, wherein said alpha carbon atom is substituted by an alkyl.

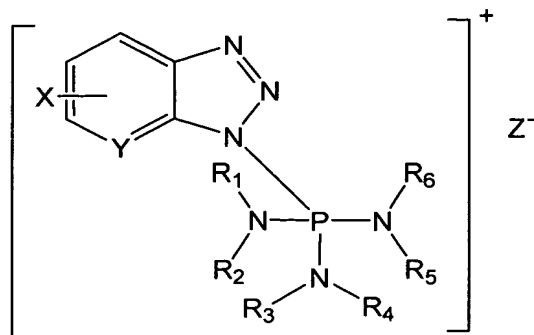
26. (Currently Amended) The crude composition of peptides of claims 21, 24 and 25, wherein said amino acid residue having said substituted alpha carbon atom is an amino isobutyric acid (aib) residue.

27. (Original) The crude composition of peptides of claim 21, wherein said peptide having said desired amino acid sequence comprises at least two coupled amino acid residues acids having an amino-containing side chain.

28. (Currently Amended) The crude composition of peptides of ~~claims 21 and 27~~ claim 21, wherein said amino acid residue having an amine-containing side chain is an arginine residue.

29. (Original) The crude composition of peptides of claim 20, being in a form selected from the group consisting of a powdered composition, a lyophilized composition, a composition bound to a solid support, a solubilized composition and a dissolved composition.

30. (Original) A compound having the general formula I:



Formula I

wherein:

X is halo;

Y is selected from the group consisting of CR' and nitrogen;

Z is an inorganic anion;

R₁-R₆ are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl and aryl, or, alternatively, at least one of R₁ and R₂, R₃ and R₄ and R₅ and R₆ forms a five- or six-membered carbocyclic ring; and

R' is selected from the group consisting of hydrogen, alkyl and cycloalkyl.

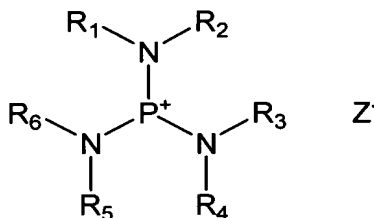
31. (Original) The compound of claim 30, being a coupling agent.
32. (Original) The compound of claim 31, being a coupling agent for use in peptide synthesis.
33. (Original) The compound of claim 30, wherein said halo is chloro.
34. (Original) The compound of claim 30, wherein each of R₁ and R₂, R₃ and R₄ and R₅ and R₆ forms a five- or six-membered carbocyclic ring.
35. (Original) The compound of claim 34, wherein each of R₁ and R₂, R₃ and R₄ and R₅ and R₆ forms a five-membered carbocyclic ring.

36. (Original) The compound of claim 30, wherein said anion is selected from the group consisting of hexahalophosphate, tetrahaloborate, trihalomethanesulfonate and bis(trihalomethylsulfonyl)imide.

37. (Original) The compound of claim 36, wherein said anion is hexafluorophosphate.

38. (Original) A process of preparing the compound of claim 30, the process comprising:

providing a compound having the general Formula II:



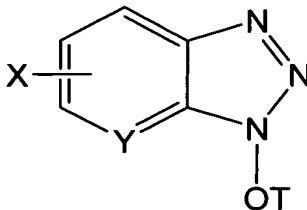
Formula II

wherein:

R₁-R₆ are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl and aryl, or, alternatively, at least one of R₁ and R₂, R₃ and R₄ and R₅ and R₆ forms a five- or six-membered carbocyclic ring; and

Z is an inorganic anion;

providing a compound having the general Formula III:



Formula III

wherein:

X is halo;

Y is selected from the group consisting of CR' and nitrogen; and

T is selected from the group consisting of hydrogen, alkyl, and cycloalkyl;

and

reacting said compound having said general Formula II and said compound having said general Formula III, thereby obtaining the compound having general Formula I.

39. (Original) The process of claim 38, wherein said reacting is performed in the presence of a base.

40. (Original) The process of claim 39, wherein said reacting is performed in the presence of an organic solvent.

41. (Original) The process of claim 38, wherein said halo is chloro.

42. (Original) The process of claim 38, wherein each of R₁ and R₂, R₃ and R₄ and R₅ and R₆ forms a five- or six-membered carbocyclic ring.

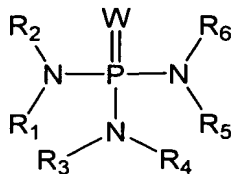
43. (Original) The process of claim 42, wherein each of said R₁ and R₂, R₃ and R₄ and R₅ and R₆ forms a five-membered carbocyclic ring.

44. (Original) The process of claim 39, wherein said anion is selected from the group consisting of hexahalophosphate, tetrahaloborate, trihalomethanesulfonate and bis(trihalomethylsulfonyl)imide.

45. (Original) The process of claim 44, wherein said anion is hexafluorophosphate.

46. (Original) The process of claim 38, wherein providing said compound having said general Formula II comprises:

providing a compound having general Formula IV:



Formula IV

wherein W is selected from the group consisting of oxygen and sulfur;

converting said compound having said general Formula IV to a phosphonium halide salt thereof; and

reacting said phosphonium halide with said Z, thereby obtaining said compound having said general Formula II.

47. (Original) A method of preparing a peptide, the method comprising:

sequentially reacting a plurality of amino acids, one with another, in the presence of the compound of claim 30, to thereby obtain a peptide containing said plurality of amino acids. .

48. (Original) The method of claim 47, wherein at least one of said amino acids is selected from the group consisting of an amino acid having a secondary alpha amine, an amino acid having a tertiary alpha amine, an amino acid having a substituted alpha carbon atom and an amino acid having an amino-containing side chain.

49. (Original) The method of claim 47, wherein at least one of said amino acids is selected from the group consisting of an amino acid having a secondary alpha amine and an amino acid having a tertiary alpha amine.

50. (Original) The method of claim 47, wherein at least one of said amino acids is an amino acid having a substituted alpha carbon atom.

51. (Original) The method of claim 47, wherein at least two coupled amino acids in said peptide are amino acids having a substituted alpha carbon atom.

52. (Currently Amended) The method of ~~claims 50 and 51~~ claim 50, wherein said alpha carbon is substituted by an alkyl.

53. (Original) The method of claim 47, wherein at least one of said amino acids is an amino acid having an amino-containing side chain.

54. (Original) The method of claim 47, wherein at least two coupled amino acids in said peptide are amino acids having an amino-containing side chain.

55. (Currently Amended) The method of ~~claims 53 or 55~~ claim 53, wherein said amino acid having an amino-containing side chain is arginine.

56. (Original) The method of claim 49, wherein said peptide is obtained in a yield greater than 10 %.

57. (Currently Amended) The method of ~~claims 50 and 51~~ claim 50, wherein said peptide is obtained in a yield greater than 90 %.

58. (Currently Amended) The method of ~~claims 53 and 54~~ claim 53, wherein said peptide is obtained in a yield greater than 80 %.

59. (Original) The method of claim 47, wherein synthesizing said peptide is effected by a solid phase synthesis.

60. (Original) The method of claim 47, wherein said halogen atom is chloro.

61. (Original) The method of claim 47, wherein each of R₁ and R₂, R₃ and R₄ and R₅ and R₆ forms a five- or six-membered carbocyclic ring.

62. (Original) The method of claim 61, wherein each of R_1 and R_2 , R_3 and R_4 and R_5 and R_6 forms a five-membered carbocyclic ring.

63. (Original) The method of claim 47, wherein said anion is selected from the group consisting of hexahalophosphate, tetrahaloborate, trihalomethanesulfonate and bis(trihalomethylsulfonyl)imide.

64. (Original) The method of claim 63, wherein said anion is hexafluorophosphate.